myc maintains embryonic stem cell pluripotency and self-renewal.

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Public Summary:
While endogenous Myc (c-myc) and Mycn (N-myc) have been reported to be separately dispensable for murine embryonic stem cell (mESC) function, myc greatly enhances induced pluripotent stem (iPS) cell formation and overexpressed c-myc confers LIF-independence upon mESC. To address the role of myc genes in ESC and in pluripotency generally, we conditionally knocked out both c- and N-myc using myc doubly homozygously floxed mESC lines (cDKO). Both lines of myc cDKO mESC exhibited severely disrupted self-renewal, pluripotency, and survival along with enhanced differentiation. Chimeric embryos injected with DKO mESC most often completely failed to develop or in rare cases survived but with severe defects. The essential nature of myc for self-renewal and pluripotency is at least in part mediated through orchestrating pluripotency-related cell cycle and metabolic programs. This study demonstrates that endogenous myc genes are essential for mESC pluripotency and self-renewal as well as providing the first evidence that myc genes are required for early embryogenesis, suggesting potential mechanisms of myc contribution to iPS cell formation.

Scientific Abstract:
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